59 Cranial Nerve I: The Olfactory Nerve

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Definitions

Hyperosmia is increased olfactory acuity, and *hypoosmia* is diminished olfactory acuity. *Anosmia,* the inability to recognize odors, may be unilateral or bilateral. *Dysosmia* is an abnormal sense of smell.

Technique

Carry a vial of a nonirritating substance in your bag; vanilla, lemon, and freshly ground coffee are good examples, and tobacco or scented soap will do if necessary. These odors stimulate the olfactory receptors. Do not use irritating odors such as camphor or menthol. These substances stimulate the trigeminal sensory receptors in addition to the olfactory receptors, potentially giving a false result.

Inform the patient that you are going to test the sense of smell. The patient places an index finger over one nostril to block it (e.g., right index finger over right nostril). He or she then closes the eyes. Instruct the patient to sniff repetitively and to tell you when an odor is detected, identifying the odor if recognized. Bring the test odor up to within 30 cm or less of the nose. Do not touch the patient when doing the test. Movement of your body will give a clue as to when the test object is being presented. Do not give auditory clues. Repeat the process with the other nostril. Smell is intact when the patient reports detection of an odor. Recognition of the odor involves olfactory memory, which is a higher cortical function.

Basic Science

The olfactory epithelium occupies about 2.5 cm^2 of area at the apex of each nostril. This patch of yellowish brown mucosa is located in a small cavity off the main nasal passage. For this reason, "sniffing" provides more rapid stimulation than normal breathing. The receptors are surrounded by nasal mucous membrane and are covered by a thin layer of moisture. There are two kinds of receptors. The first kind consists of trigeminal nerve fibers that are sensitive to irritating substances and temperature; the neuroanatomy is similar to that of pain and temperature receptors elsewhere in the body.

The second kind of receptor consists of olfactory nerve cells, which form the receptor for olfaction. The soma, or body, of the cell lies in the olfactory epithelium. Olfactory epithelium is a primitive type of sensory epithelium, lending support to the concept that olfaction is phylogenetically the oldest of the senses. The cell is both a receptor and a bipolar first-order neuron. A single dendrite projects from the apical pole of the cell to the surface of the epithelium. This dendrite ends in an apical dendritic knob (olfactory knob). Each knob gives rise to 5 to 20 long delicate nonmotile cilia, which extend into the mucus covering the sensory epithelium. The olfactory neuron, unlike most other neurons, has a life span of only 30 to 40 days. New neurons differentiate from stem cells in the deepest or basal region of the olfactory epithelium. The basal pole of the neuron gives rise to a single unmyelinated axon. The axons form bundles, sheathed in Schwann cells, and pass through the cribiform plate to synapse in the olfactory bulb. The axons are collectively known as the olfactory nerve.

The detection threshold for odorants is quite low: 10^{-13} to 10^{-4} in air. Studies suggest that the volume concentration of receptor molecules in the mucus is in the range of 10^{-5} M. Each olfactory neuron has about 10^6 receptor molecules on its cilia. Odors penetrate the mucus overlying the sensory epithelium and gain access to the receptors by virtue of their partition and diffusion coefficients in the olfactory mucus. An odorant traverses the mucus in the range of a few dozen milliseconds, and forms a complex with the receptor in about the same time span. The odorant molecule combines with integral membrane proteins that form the receptor. The proteins and odorant-gated channels that mediate sensory transduction are located in the membranes of the olfactory cilia and the apical dendritic olfactory knob. Voltage-gated channels, located in the initial axonal segment and the axolemma, are associated with impulse initiation and propagation. The second messenger system is probably a G protein-adenylate cyclase cascade. The precise mechanisms leading to detection and identification of odors is an area of active, vigorous research. Figure 59.1 illustrates a possible molecular model for olfactory reception.

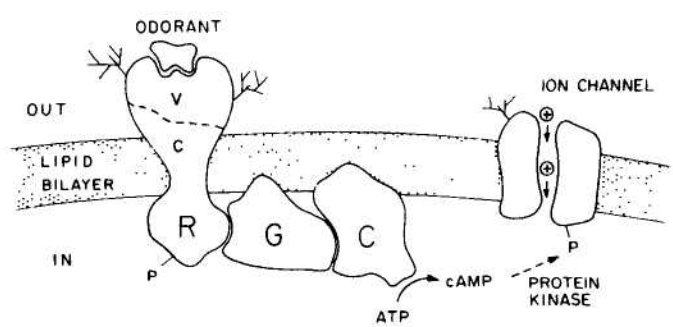

Figure 59.1
A most probable molecular model for olfactory reception and transduction. The receptor molecule (R) is an integral membrane glycoprotein with a constant (c) and a variable (v) region. The odorant-occupied receptor activates a GTP-binding protein or G-protein (G), which modulates the activity of adenylate cyclase (C), an enzyme that produces the second messenger, cyclic AMP (cAMP). The latter molecule activates cAMP-dependent protein kinase to cause phosphorylation of other proteins. Phosphorylation (p) of ion channel polypeptides causes membrane potential changes, while that of the receptor polypeptide constitutes a feedback mechanism underlying adaptation. *From* Lancet D. Vertebrate olfactory reception. Annu Rev Neurosci 1986;9:329–55. Used with permission.

The structure of the olfactory bulb is quite complex. The structural units are discrete spherical bodies, the glomeruli, about 0.2 mm in diameter. Axons from the olfactory cell (first-order neuron) synapse in the glomeruli with the primary dendrites of the mitral cells (second-order neuron). The number of receptors that converge on the mitral cell is very large, about 100:1. Other cell types in the bulb include the tufted cells, whose dendrites also participate in synaptic connections in the glomeruli. The olfactory bulbs apparently participate extensively in the processing of olfactory information. There are at least five feedback loops and other interconnections within the bulb. There are connections with the other olfactory bulb via the anterior commissure. Centrifugal fibers conveying impulses from the brain influence the activity of the bulb. The bulb apparently follows the neural organization of the visual and other sensory systems. There is an interplay of inhibitory and excitatory mechanisms acting to process incoming information under the efferent influence of the cortex.

Axons leave the olfactory bulb as the olfactory tract. Tufted cell axons mainly pass laterally to the anterior commissure and then to the contralateral olfactory bulb. Mitral cell axons project centrally. The central areas to which the olfactory bulb projects include the anterior perforated space, the amygdaloid nucleus, and the cortex of the piriform lobe. There are secondary and tertiary connections with various other areas, including the limbic system.

Clinical Significance

Hyperosmia, or lowered threshold for odors, occurs with Addison's disease and mucoviscidosis. Clinical perception of hyperosmia is ordinarily just about impossible either by history taking or by bedside testing.

Hypoosmia is usually caused by local processes that involve both the nasal and olfactory mucosa. Examples include rhinitis due to the common cold or allergy, smoking, certain industrial fumes, and intranasal polyps or carcinoma. Pernicious anemia, diabetes, and vitamin A deficiency cause diminished olfactory acuity. Pernicious anemia can also cause anosmia. Hypoosmia can occur after total laryngectomy. The reasons are not known.

Anosmia may be bilateral or unilateral. The patient can recognize bilateral anosmia, but unilateral anosmia is usually not perceived. Head trauma is probably the most frequent cause, with an incidence of 7.5% in one large series. Blows to the occiput are five times more likely to produce anosmia than blows to the forehead because of the contrecoup effect. The injury can be so trivial as to go almost unnoticed. Tumors of the floor of the anterior fossa, such as meningiomas of the sphenoid ridge or olfactory groove, can produce anosmia, which is usually unilateral. Meningitis or abscess associated with osteomyelitis of the frontal or ethmoid bones can produce anosmia. Congenital absence of smell is present in albinos. Subarachnoid hemorrhage can cause anosmia. Hysteria is another cause for anosmia. Hysteria can be identified by comparing perception for coffee or vanilla with ammonia perception. Coffee and vanilla principally stimulate the olfactory cell receptors. Ammonia is a trigeminal nerve stimulator. In anosmia of organic cause the ammonia can be detected but the coffee or vanilla odor cannot.

A number of neurological diseases cause *dysosmia,* or dysfunction of smell: Alzheimer's disease, Korsakoff's psychosis, Huntington's chorea, and Parkinson's disease.

Table 59.1
Examples of Disorders Reported To Be Associated with Olfactory Dysfunction

Endocrine
- Adrenal cortical insufficiency
- Cushing's syndrome
- Diabetes mellitus
- Hypothyroidism
- Kallman's syndrome
- Primary amenorrhea
- Pseudohypoparathyroidism
- Turner's syndrome

Local diseases and mechanical obstruction of the airways
- Adenoid hypertrophy
- Allergic rhinitis
- Atrophic rhinitis (Ozena)
- Bronchial asthma
- Deformity secondary to trauma
- Exposure to toxic chemicals
- Leprosy
- Malignant disease of paranasal sinuses with extension into the nasal cavities
- Nasal polyposis
- Sinusitis
- Sjogren's syndrome
- Tumors of the nasopharynx with extension into the nasal cavities
- Vasomotor rhinitis

Neurologic
- Alzheimer's disease
- Epilepsy
- Head trauma
- Huntington's chorea
- Intracranial surgery
- Multiple sclerosis
- Parkinson's disease

Nutritional
- Chronic renal failure
- Cyanocobalamin (vitamin B_{12}) deficiency
- Korsakoff's psychosis

Psychiatric
- Depression
- Olfactory reference syndrome
- Schizophrenia

Tumors
- Intracranial:
  - Aneurysms of the anterior communicating bifurcation
  - Frontal lobe glioma
  - Hydrocephalus
  - Internal carotid aneurysms extending over the pituitary fossa
  - Neuroblastoma
  - Suprasellar meningioma
  - Sphenoidal ridge meningioma
  - Other meningiomas
- Intranasal:
  - Adenocarcinoma
  - Inverted papilloma
  - Melanoma
  - Squamous cell carcinoma

Viral and infectious
- Acute viral hepatitis
- Herpes simplex
- Influenza-like infections

Source: From Doty RL, Kimmelman CP. Smell and taste and their disorders. In: Asbury AK, McKhann GM, McDonald WI, eds. Diseases of the nervous system. Philadelphia: W.B. Saunders, 1986;469.

Pathologic changes in the olfactory system may be among the earliest changes in Alzheimer's disease. Olfactory hallucinations, usually of unpleasant odors such as burned rubber, can occur in epilepsy, withdrawal states, and certain psychiatric conditions. The amygdala may be the source of these hallucinations.

A valuable clinical corollary is that the patient often reports hypoosmia and anosmia as a decreased or absent ability to taste food. For example, pernicious anemia is a leading possibility in an elderly patient with spastic paraparesis and anemia who complains that he or she no longer enjoys eating because food does not taste the same.

Table 59.1 is a summary of disorders associated with olfactory dysfunction.

References

Doty RL, Kimmelman CP. Smell and taste and their disorders. In: Asbury AK, McKhann GM, McDonald WI, eds. Diseases of the nervous system. Philadelphia, W.B. Saunders, 1986;466–78.

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